

In the Specification:

Please replace the title with the following title:

VANILREP4 POLYPEPTIDES

Please replace page 2, lines 23-27 with the following paragraph:

Polypeptides of the present invention are believed to be members of the ion channel family of polypeptides. They are therefore of interest because they are related to the VR1 channel which is associated with the mechanism of action of capsaicin (a vanilloid compound), a constituent of chilli peppers. Capsaicin elicits a sensation of burning pain by selectively activating sensory neurons that convey information about noxious stimuli. ~~to the ee~~

Please replace page 10, lines 4-29 with the following paragraph:

The polynucleotide sequence of SEQ ID NO:1 shows homology with rat vanilloid receptor, VR1 (M. J. Caterina et al., Nature 389: 816-824, 1997). The polynucleotide sequence of SEQ ID NO:1 is a cDNA sequence that encodes the polypeptide of SEQ ID NO:2. The polynucleotide sequence encoding the polypeptide of SEQ ID NO:2 may be identical to the polypeptide encoding sequence of SEQ ID NO:1 or it may be a sequence other than SEQ ID NO:1, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes the polypeptide of SEQ ID NO:2. The polypeptide of the SEQ ID NO:2 is related to other proteins of the ion channel family, having homology and/or structural similarity with ~~with~~ rat vanilloid receptor, VR1 (M. J. Caterina et al., Nature 389: 816-824, 1997). The nucleotide sequence of SEQ ID NO:4 is a cDNA sequence and comprises a polypeptide encoding sequence (nucleotide 90 to 2705, Exon 1 (< 1-58), Exon 2 (59-475), Exon 3 (476-648), Exon 4 (649-801), Exon 5 (802-942), Exon 6 (943-1241), Exon 7 (1242-1421), Exon 8 (1422-1580), Exon 9 (1581-1673), Exon 10 (1674-1747), Exon 11 (1748-1913), Exon 12 (1914-1980), Exon 13 (1981-2297), Exon 14 (2298-2425), Exon 15 (2426-2546), Exon 16 (2547 - >3237)) encoding a polypeptide of 871 amino acids, the polypeptide of SEQ ID NO:2. Knowledge of the intron-exon structure of VANILREP4 can be used for mutation screening, for example as a diagnostic test for diseases which may be caused by alterations of VANILREP4. The screening of genomic DNA is desirable for the analysis of non-coding regions, such as upstream regulatory regions and intron splice sites. It is also useful in cases where mRNA is not readily available for mutation analysis. Knowledge of the genomic structure is also important for the generation of animal models. Such models may be used to study the function of VANILREP4 and for drug screening studies. For example, mouse knock-out models typically have a selection marker, which upon insertion into a coding exon, ablate the functioning of the targeted allele.

The genomic structure may also be useful in analysing possible splice variants of VANILREP4. Splice variants are important because they may have different functions and different expression patterns.

Please replace page 5, lines 33-36 with the following paragraph:

The present invention also relates to partial or other polynucleotide and polypeptide sequences which were first identified prior to the determination of the corresponding full length sequence of SEQ ID NO4. Accordingly, in a further aspect, the present invention provides for an isolated polynucleotide which:

Please replace page 11, lines 4-29 with the following paragraph.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequence is specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an important first step in correlating those sequences with gene associated disease. Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillelt, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, Nature Genetics 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (Hum Mol Genet 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillelt D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. ~~This comparison is conducted at~~
~~http://www.genome.wi.mit.edu/~~ The gene of the present invention maps to human chromosome 12q24.1.

Please replace page 20, lines 19-26 with the following paragraph:

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215, 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at www.ncbi.nlm.nih.gov) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99, 1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448, 1988, available as part of the Wisconsin Sequence Analysis Package).

Please replace page 23, lines 9-11 with the following lines:

VR-4 labelled probe:	5'-ATGAGGACCAGACCAACTGCA _____ (SEQ ID NO:5)
VR-4 forward primer	5'-GGAGGAAGGTGCTGAAGGTCTC _____ (SEQ ID NO:6)
VR-4 reverse primer	5'-CACTTACCCCTCGTGCCGTGACAG _____ (SEQ ID NO:7)